REMARKS/ARGUMENTS

I. Status of the Claims

Claims 4, 6-8, 17, 20-28, 34 and 36-38 are pending in the application.

Claims 4, 6-8, 17, 20-28, 34 and 36-38 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Maertens et al. (WO 96/13590, 9 May 1996) or Maertens et al. (US 2002/0183508 Al, December 5, 2002) or Selby et al. (J. *Gen. Virol.* **74**:1103-1113, 1993) or Donnelly et al. (WO 97/47358, 18 December, 1997) in view of Liao et al. (WO 96/38474), Tokushige et al. (*Hepatology* **24**:14-20, 1996) and Ferrari et al.(*Hepatology* **19**:286-295). The rejection of claims 4, 6, 8, 17, 34, 36, and 38 under 35 U.S.C. § 102 has been withdrawn.

II. The claims are patentable under 35 U.S.C. § 103(a)

Claims 4, 6-8, 17, 20-28, 34 and 36-38 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Maertens et al. (Maertens et al. WO 96/13590, 9 May 1996) or Maertens et al. (Maertens et al. US 2002/0183508 Al, December 5, 2002) or Selby et al. (J. *Gen. Virol.* **74**:1103-1113, 1993) or Donnelly et al. (WO 97/47358, 18 December, 1997) in view of Liao et al. (WO 96/38474), Tokushige et al. (*Hepatology* **24**:14-20, 1996) and Ferrari et al. (*Hepatology* **19**:286-295). Applicants traverse the rejection.

To establish a *prima facie* case of obviousness, there must be some suggestion or motivation to modify the reference or to combine the reference teachings, there must be a reasonable expectation of success for achieving the claimed invention and its particular results, and the prior art must teach or suggest all the claim limitations. *See In re Vaeck*, 20 U.S.P.Q. 2d 1438 (Fed. Cir. 1991). For the reasons discussed below, a proper *prima facie* case of obviousness has not been set forth.

Independent claims are 6, 17 and 34. Independent claim 6 is directed to a recombinant nucleic acid molecule comprising a nucleotide sequence encoding a fusion protein of hepatitis C virus NS4 or NS5 protein or any combination thereof, wherein the nucleotide sequence is operably linked to regulatory elements, the regulatory elements comprising a promoter, enhancer, polyadenylation sequence, and a 5' untranslated region (5'-UTR), the 5'-UTR comprising at least the 9 most 3' nucleotides of a 5' UTR of hepatitis C virus. Independent claim 17 is directed to a method of inducing an immune response against hepatitis C virus in a human uninfected by hepatitis C virus comprising administering to the

human a recombinant nucleic acid molecule comprising a nucleotide sequence encoding a fusion protein of hepatitis C virus nonstructural proteins NS3, NS4, or NS5, or any combination thereof, in an amount effective to induce an immune response against hepatitis C virus. Independent claim 34 is directed to a recombinant nucleic acid molecule comprising a nucleotide sequence encoding a hepatitis C virus fusion protein encoding NS3 or a combination of NS3 with NS4 or NS5, or a combination of NS3 with both NS4 and NS5, wherein the nucleotide sequence is operably linked to a promoter, enhancer, polyadenylation sequence, and the entire 5' UTR of hepatitis C virus or a fragment thereof including the last nine nucleotides of the hepatitis C virus 5' UTR. The cited references fail to teach or suggest such a method or a recombinant nucleic acid molecule.

The Office Action cites the Maertens et al. reference (WO 96/13590) and the Maertens et al. reference (US 2002/0183508 Al) as allegedly teaching a recombinant expression vector comprising a polynucleotide comprising sequences that express NS4, NS5 and also comprise 5'-UTR of hepatitis C virus, the Selby et al. reference as allegedly teaching several constructs for expression of viral proteins, for example, plasmids pHCV5-1 and pHCV comprising the entire 5'UTR and 3'UTR and the coding sequence for the non-structural proteins, and the Donnelly et al. reference as allegedly teaching synthetic hepatitis C genes, pharmaceutical formulations and formulations for vaccination and gene therapy. By contrast, the presently claimed method of inducing an immune response and claimed recombinant nucleic acid molecule comprises a hepatitis C virus fusion protein encoding NS4 or NS5, or NS3, NS4, or NS5, or any combination thereof or a fusion protein encoding NS3 or a combination of NS3 with NS4 or NS5, or a combination of NS3 with both NS4 and NS5. The cited references do not refer to such a fusion protein, but rather teach "a polynucleotide of ... the NS4 or the NS5B region or a part thereof" or "a part of the NS5 gene nucleotide sequence." See, for example, claims 7, 8, 28 or 29 of Maertens et al., WO 96/13590 or US 2002/018305. The Selby et al. reference, as cited by the Examiner, allegedly teaches that plasmid pHCV5-1 contains an "8706 base pair fragment from the C9000 cDNA clone" of the HCV polyprotein. See for example, Selby et al., page 1104, column 1 and Figure 1. Similarly, the Donnelly et al. reference allegedly teaches a synthetic hepatitis C genes, pharmaceutical compositions and formulations for vaccination. See for example, claim 1 of the Donnelly et al. reference. The polynucleotides as taught by the Maertens et al. references,

the Selby reference, and the Donnelly et al. reference do not teach or suggest the presently claimed method or recombinant nucleic acid molecule encoding a fusion protein of hepatitis NS4 or NS5, or NS3, NS4, or NS5, or a combination thereof. Furthermore, the Liao et al. reference, Tokushige et al. reference, Ferrari et al. reference and Diepolder et al. reference do not provide any additional teaching or suggestion to cure the deficiencies of the primary references cited. The examiner cites these references for allegedly teaching diagnosis of and vaccination against hepatitis C virus, a method of producing immune response to hepatitis C core virus, or T cell response to hepatitis C antigens. These additional references cited by the office action fail to cure the deficiencies of the Maertens et al. references, the Selby et al. reference, or the Donnelly et al. reference. Accordingly, even if an ordinarily skilled artisan would have found some reason to combine the teachings of the references, the claimed method would not have been achieved. The combination of references do not teach or suggest applicants' claimed invention, in part, a recombinant nucleic acid molecule comprising a hepatitis C virus fusion protein encoding NS4 or NS5, or NS3, NS4, or NS5, or any combination thereof or a fusion protein encoding NS3 or a combination of NS3 with NS4 or NS5, or a combination of NS3 with both NS4 and NS5, or applicants' claimed invention which uses these recombinant nucleic acid molecules in a method of inducing an immune response to hepatitis C virus in a human.

Furthermore, the combination of references do not teach or suggest applicants' claimed invention, in part, a recombinant nucleic acid molecule, as above, wherein the nucleotide sequence encodes a fragment of at least 50 amino acids of NS4 or NS5 or wherein the promoter is a cytomegalovirus promoter and the enhancer is a Rous Sarcoma Virus enhancer. The combination of references do not teach or suggest applicants' claimed invention, in part, a recombinant host cell comprising the recombinant nucleic acid molecule, as above.

Furthermore, the combination of references do not teach or suggest applicants' claimed invention, in part, a method of inducing an immune response against hepatitis C virus in a human uninfected by hepatitis C virus, as claimed, wherein the nucleotide sequence encodes a fragment of at least 50 amino acids of nonstructural protein selected from the group consisting of NS3, NS4, and NS5. Furthermore, the combination of references do not teach or suggest applicants' claimed invention, in part, the claimed method wherein the

nucleotide sequence is operably linked to regulatory elements functional in human cells, for example, operably linked to a promoter, enhancer, polyadenylation sequence, and optionally 5' UTR of hepatitis C virus. Furthermore, as claimed, the promoter is a cytomegalovirus promoter and the enhancer is a Rous Sarcoma Virus enhancer. Furthermore, the claimed method comprises an immune response, a cellular immune response or a humoral immune response. Furthermore, the recombinant nucleic acid molecule is in a pharmaceutical composition comprising a pharmaceutically acceptable carrier or diluent. The pharmaceutical composition further comprises a facilitator, and further wherein the facilitator is bupivacaine. Therefore, the combination of references cited do not teach or suggest applicants' claimed invention, in part, a recombinant nucleic acid molecule, or the claimed method of inducing an immune response against hepatitis C virus in a human comprising administering the recombinant nucleic acid molecules.

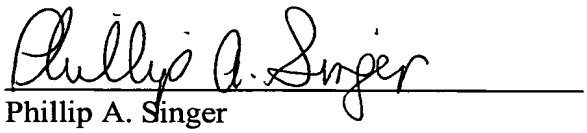
Accordingly, applicants respectfully request that the rejection of claims 4, 6-8, 17, 20-28, 34 and 36-38 under 35 U.S.C. § 103(a) be withdrawn.

VI. Conclusion

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-332-1380.

Date: July 9, 2004



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